

Peer Review File

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Reviewer A

The authors performed a good study on the placement of prosthetic implants during REZ decompression, which is important in microvascular decompression surgery for hemifacial spasm.

Annoying is a term. The terms "in-situ" and "REZ-disturbing group" are not yet defined exactly. The term "REZ-undisturbing group" was also used. The difference in "disturbing" seems to be the difference between placing teflon in REZ or not. Is there any better term?

Author response: Yes, the difference between the two decompression strategies is the difference between placing implants in REZ or out of it. This comment helped us get the point. The terms "in-situ" and "REZ-disturbing" are actually somewhat incomprehensible. In the revision, we tried to express this in a more direct way with "implants contacted REZ" and "implants did not contact REZ" to represent the relationship between implanted pads and REZ. And the two strategies "in situ" and "REZ-disturbing" have been replaced by "REZ-contact" and "REZ-non-contact" respectively.

Since there is no difference in long-term effectiveness between the REZ-undisturbing group and the REZ-disturbing group, I believe that the REZ-undisturbing group should not lead to a better method. The authors need to express their opinions clearly. However, it should be concluded that REZ-undisturbing surgery is a slightly better method ONLY IF the result is the same but if there is more immediate spasm-free and less complication.

Author response: We agree with the reviewer. Purely from the statistics, the REZ-undisturbing strategy (REZ-non-contact procedure in the revision) has a higher complete cure rate in the early postoperative period. But, in terms of long-term outcomes and the applicability and potential risks of these two strategies, the REZ-undisturbing has no obvious advantage. Therefore, there is no need to deliberately place the pad outside REZ without contacting this area. And we made this opinion clear in the Conclusion (see Page 3, line 33-38; Page 19-20, line 300-308 in clean version). (see Page 3, line 89-94; Page 19-20, line 1270-1344 in the version with tracked changes)

It seems that the authors performed in-situ decompression only when REZ-undisturbing surgery was dangerous or difficult due to the presence of a perforator. Please clearly state in the methods in which cases the authors perform in-situ/REZ-undisturbing surgery.

Author response: Thanks. This has been described in the original manuscript, but we have not sufficiently made this clear. The in-situ and REZ-undisturbing (REZ-contact and REZ-non-contact in the revision) surgery were performed in different periods. That is, we always used the in-situ (REZ-contact) decompression before the end of the year 2017. From the end of 2017 to the beginning of 2018, we began to implement REZ-undisturbing (REZ-non-contact) procedure. Because at that time, we supposed that the complete decompression without contacting REZ might be better. So, the cases before 2018 were mainly classified into in-situ surgery group and the cases in 2018 were more likely to be classified into REZ-undisturbing group according to the surgery procedure they received. Then we reviewed all the included patients, the cases in which the REZ-undisturbing (REZ-non-contact) strategy was inapplicable due to the presence of an immovable perforator were kicked off (see the description in page 7, line 107-111 in clean version, and page 7, line 391-395 in the version with tracked changes), they were not included in in-situ group. If not kicked off, these cases may affect the comparability of the neurovascular complexity in two groups.

In the revised version, we redefined the inclusion and exclusion criteria more clearly (see page5, line 67-80 in clean version, and page 5, line 273-286 in the version with tracked changes).

Line 47; Teflon is not placed between the offending vessel and medulla oblongata. It should be described as Supraolivary fossa (or pontomedullary sulcus).

Author response: Thanks for pointing this out. The "medulla oblongata" in the manuscript has been replaced by "Supraolivary fossa" (see page1, line 10 in clean version, and page 1, line 10 in the version with tracked changes)

Line 106; Lateral spread response (LSR) is the correct term rather than abnormal muscle response (AMR).

Author response: Thanks for pointing this out. The "abnormal muscle response (AMR)" in the manuscript and Table 1 have been replaced by "Lateral spread response (LSR) "

Line 106; The authors applied facial EMG and facial motor evoked potential during surgery, but there is no description as to whether lateral spread response (LSR) was used as the completeness of decompression.

Author response: Sorry for this omission, the description "disappearance of LSR was used as an indication for decompression completion" has been added in the part of Methods (see page 8, line 115-118 in clean version, and page 8, line 448-451 in the version with tracked changes). But the LSR is not taken as an absolute standard for complete decompression, because in few cases, the operator has repeatedly confirmed that there was no responsible vascular compression on REZ, but the LSR was still exist (with decreased amplitude), and after the operation, the spasm disappeared completely.

The definition of recurrence of HFS MVD is that spasm occurs again after 1-year spasm-free after surgery. If there is spasm within 1 year after surgery, it should be interpreted as failure. What is the opinion of the authors?

Author response: We partially agree with this opinion. Since most of the patients (16/17 in in-situ group, 6/7 in RZE-undisturbing group) who suffered early reemergence achieved complete cure again within 1 year, we tend to use "reappearance" instead of "recurrence" or "failure" to describe this phenomenon. While, there were 2 cases (1 in in-situ group and 1 in RZE-undisturbing group) who experienced a persistent but alleviated spasm after a few days complete relief that should be interpreted as partial relief. These results and opinions have been added in the revision (see page 11-12, line 174-178 in clean version, and page 11-12, line 679-784 in the version with tracked changes)

Reviewer B

Very impress by your experience, 229 hemifacial spasms operated on in 2 years, no question about your expertise.

Clinical outcomes are well analyzed and clear (Fig 3,4,5,6,7)

Despite the excellent format they are two weak points concerning the content.

1- the goal of the work is a comparative study between "undisturbing" and "in situ" technical nuances for facial nerve decompression. indeed, it is "nuance" on the Figure 1 without reading the legend, "understurbing" and " in situ" pictures can be confused. The "undisturbing" fig 1F shows vascular structures mobilized and disturbed from their offending contact and maintained in such position by polyester pads with the REZ still visible. In both procedures the delicate and useful maneuver is the same, it is to "disturb" the neurovascular conflict and the positioning of pads is much more linked with the anatomical course of the vessels than a rational strategy. Of course, you know that, but this is not clearly written.

Author response: Thanks for pointing this out, we now have also realized that the words "in situ" and "undisturbing" are confused, and it is inappropriate to use "undisturbing" to represent the non-contact relationship between the implanted pads and REZ. In the revised version, we tend to use "implants contacted REZ" and "implants did not contact REZ" to describe the relationship between the pads and

REZ, and use "REZ-contact" and "REZ-non-contact" to represent the two procedures respectively. The figures and tables have been revised accordingly.

In both procedures, the neurovascular conflict was disturbed, the difference is the placement of pads and the translocation of offending vessels. And, yes, in certain circumstances, the offending vessel can't be moved freely, especially when it goes through the facial-vestibulocochlear nerve complex or has a tension perforator. And the pads are normally placed along with the anatomical course of the offending vessel. But in many cases, the offending vessels could be moved gently away from REZ, and the "REZ-non-contact" procedure is applicable. This has been mentioned in the original Methods, we have rewritten and clarified this (see page 7, line 102-111 in clean version, and page 7, line 386-395 in the version with tracked changes), and also added some more detailed discussion in the revision (see page 14, line 214-220 in clean version, and page 14, line 900-906 in the version with tracked changes).

2- Curiously your manuscript on neurovascular decompression don't mention any offending vascular structure. The offending artery (ies) is an important factor for the result as well as the distortion of the neural structures. How we can appreciate the results of such subtle technical nuances without consideration of the offending vessel.

Author response: We agree with your opinion. The complex structure of responsible vessels may directly affect the MVD outcomes regardless of compression procedures. In order to ensure the comparability of neurovascular complexity between the two groups, cases in which neurovascular conflicts were beyond REZ and cases in which only REZ-contact decompression can be performed due to the immovable structure of offending vessels were excluded. (see page 7, line 107-111 in clean version, and page 7, line 392-395 in the version with tracked changes) These exclusions, to some extent, indicate the limitation of applying REZ-non-contact procedure (undisturbing strategy in original version).

The major criticism is your final message could be understood as the following: if you don't mobilize too much the vessels or if you don't touch the vessels the result will be good or even better. We know that it is incorrect. and I am convinced this is not your recommendation because you emphasize that the "undisturbing" surgical is longer and can induce facial weakness as well as "in-situ" nuance.

Author response: We did not make this clear. The term "in-situ" was intended to mean that the implants were placed within the area of facial REZ and have contact with it, "undisturbing" was intended to mean that the implants were placed outside REZ without contacting it. In the revised version, "REZ-contact" and "REZ-non-contact" have been used to describe the two surgical procedures. The conclusion has been

clarified as "REZ-non-contact decompression procedure showed superiority in short-term postoperative outcomes. However, not all patients are suitable for REZ-non-contact decompression, and the long-term outcomes were similar in the 2 procedures. Given its limitations and potential risks, the REZ-non-contact procedure can be used as an alternative individualized strategy in MVD, and there is no need to pursue REZ-non-contact during the decompression." in the revised version (see page 3, line33-38 in clean version, and page 3, line 89-94 in the version with tracked changes).

lines 144-162 clinical outcomes are complicated to follow please use the same as you did in table 1 and supplement

Author response: This has been amended and the results have been rewritten with more detailed descriptions. (see page 9-13, line 136-201 in clean version, and page 9-13, line 488-837 in the version with tracked changes)

-Undisturbing group: complete recovery N, %; partial recovery N, %; reappeared N, %
- in situ

Author response: This has been amended (see page 10-11, line 151-155, 162-166, 170-176 in clean version, and page 10-11, line 572-576, 667-671, 675-681 in the version with tracked changes)

line 157 a small number? the number please

Author response: The number has been added (see page 11-12, line 176-178 in clean version, and page 11-12, line 681, 783-784 in the version with tracked changes).

line 166 complications Please the data first, then the comments

Author response: The data and the detailed description of complications has been added (see page 12-13, line 183-201 in clean version, and page 12-13, line 789-798, 829-837 in the version with tracked changes).

line 176 the references 2, 26 are from 2008 and 2011, it was already well known and has been extensively described for 50 years

Author response: Thanks for pointing this out. In regard to the original research on REZ, these two references are indeed inappropriate. We have modified our description to highlight the anatomical features of REZ and cited classic researches

focused on REZ (see page 13, line 204-206 in clean version, and page 13, line 840-842 in the version with tracked changes).

line 184 references concern only vertebral a. To stress the importance to mention the offending vessels

Author response: Reference 19 and 29 were not accurate. The incorrect references were deleted (see page 14, line 211 in clean version, and page 14, line 897 in the version with tracked changes)

line 191 and 227 "harassment" to the REZ must be avoid 1- there is no reason, 2- this is for all cases

Author response: This has been amended, and "avoiding harassment to the REZ" has been replaced by "irritation" and "avoiding implants contact with REZ" (see page 15, line 228, 230 in clean version, and page 15, line 1050, 1052 in the version with tracked changes)

line 197 "REZ-undisturbing strategy not applicable if perforating artery". What is your management. Do you recommend or not coagulation of such artery?

Author response: Coagulation of such artery may lead to catastrophic complications of ischemic infarction. We do not recommend.

If the perforating vessel restricts the replacement of responsible vessels, an in-situ decompression will be performed, and the pad inserted to separate the responsible vessels and REZ should be small and avoid causing excessive tension.

line207 Can you explain Why REZ-undisturbing group is longer as surgical time? It should be shorter?

Author response: It is undeniable that the offending vessels in REZ-undisturbing strategy usually have to be removed away very gently from facial nerve and the implants sometimes need to be adjusted many more times, which, to some extent, increased the surgical time. The possible explanation has been added. (see page 14-15, line 220-226 in clean version, and page 14-15, line 906-910, 1047-1048 in the version with tracked changes)

We have reconsidered this, the time described in the manuscript is the total operation time, not just the time under the microscope. Accurately, the total operation time is not suitable to represent the exact time of the two strategies. So, we are considering to delete the "operation time".

line 220 Nowadays facial weakness and hearing loss are not acceptable for functional surgery. This is out of the topic here, but what is the value of facial and cochlear monitoring? This is a question to the authors only.

Author response: During MVD, facial and cochlear monitoring are extensively used to protect facial and vestibulocochlear nerve from being damaged by surgical manipulations, especially direct mechanical damage. But BAEP monitoring were more likely to report hearing loss in MVD for trigeminal neuralgia but not for HFS (Bartindale, et al. 2018). Nowadays severe facial palsy and permanent hearing loss or deafness are rare and not acceptable, but mild and transient facial weakness and hearing deficits are commonly reported, and the etiology varied, including surgical disturbance, heterogeneous stimulation of implants, viral reactivation and delayed neurological edema. Operative facial and cochlear monitoring can warn the surgical trauma to the nerve, but it can't prevent the postoperative facial palsy and hearing loss.

line 229 delayed facial palsy after 8 to 10 postoperative days is a viral reactivation with a complete recovery within the month. This has been demonstrated in ENT literature

Author response: The viral reactivation as a possible mechanism for delayed facial palsy has been added in the part of Discussion (see page 18, line 276 in clean version, and page 18, line 1221 in the version with tracked changes).

We reviewed the related literature and noted that the causality between viral reactivation and delayed facial palsy has not been well determined. Some researchers (Franco-Vidal, et al. 2004; Furuta, et al. 2000; Gianoli 2002) reported that the development of delayed facial palsy is closely related to the increased IgM titers of herpes simplex virus (HSV) and varicella zoster virus (VZV), while in some large sample studies (Han, et al. 2012; Rhee, et al. 2006), no correlation was found between viral activation and delayed facial palsy. We think the etiology of delayed facial palsy and its association with viral reactivation should be further clarified.

line 247 transient hearing loss, you are lucky to get some recovery

Author response: As you have mentioned above, severe and permanent hearing loss is not acceptable for functional surgery. But hearing loss in this manuscript was more about hearing decrease caused by fluid entering the mastoid air cells and can gradually recover. To clearly address this issue, we added a paragraph to discuss the etiology and recovery of the transient hearing loss (see page 16, line 244-253 in clean version, and page 16, line 1121-1130 in the version with tracked changes)

There may be a matter of comprehending the phrase of "hearing loss". The phrase used to describe the auditory deficiency after MVD varied in publications, like

hearing loss (Bartindale, et al. 2018), hearing impairment (Jung, et al. 2017), hearing decrease (Sindou and Mercier 2018) and hearing deficits (Murai, et al. 1991). There is no distinction between these phrases in terms of severity, and many studies relied on subjective measures of reporting hearing loss.

line 258 again not comprehensible in your hand. How you explain transient facial paralysis. The facial nerve is out of the decompression maneuvers and protect by the auditory.

Author response: Thanks for pointing this out. In the revised version, we added a paragraph in the part of Discussion and tried to explain the occurrence of facial paralysis (see page 17-18, line 257-275 in clean version, and page 17-18, line 1175-1190, 1218-1223 in the version with tracked changes). Without heterogeneous stimulation of implants, the REZ-non-contact group ("REZ-undisturbing group" in the original manuscript) certainly has lower incidence of facial palsy, but it still has 5 facial palsy cases. The possible reasons we think could be preoperative acupuncture, viral reactivation and microcirculation disturbance due to vasospasm.

Conclusion the message of your conclusion could be understood at the opposite of which you would like to demonstrate. It could be the following: If you don't disturb the REZ where is the neurovascular conflict you can get better result. Of course, we never disturb the REZ of the facial nerve in any cases, but we always have to dislocate the neurovascular conflict acting on the offending structures. What do you mean by REZ-undisturbing as it is described and what the reader understands, it is not the same, especially if it is not already familiar with the procedure? This must be clarifying. You have very good result with the "two technical nuances", and the results are very similar as it was in fact two subtle aspects of the same surgical procedure.

Each surgeon must adapt his procedure to the patient and the operative finding., it is not necessary so different in fact.

In my opinion such data deserve much better than confusing "technical nuances" you should redefined and enlarged the orientation of your manuscript.

Author response: Thanks very much, these comments are valuable and pertinent, they help a lot.

First, we realized that the two decompression procedures as well as their difference were not clearly described. In the original manuscript, the term "in-situ" was intended to mean that the implants were placed within the area of facial REZ and have contact with it, "undisturbing" was intended to mean that the implants were placed outside REZ without contacting it. But we did not make them clear, and the words themselves are somewhat ambiguous and incomprehensible. In the revised version, we tend to use "implants contacted REZ" and "implants did not contact REZ" to describe the

positional relationship between the implants and facial REZ directly, and use "REZ-contact procedure" and "REZ-non-contact procedure" to differ the two procedures.

Second, unclear conclusion. The previous conclusion was more like a summary of the results. In the revised version, we clarified the conclusion with the following description: "REZ-non-contact decompression procedure has superiority in short-term postoperative outcomes. But the long-term outcomes were similar in these two procedures. Given its limitations and potential risks, the REZ-non-contact procedure can be used as an alternative individualized strategy in MVD, and there is no need to pursue REZ-non-contact during the decompression". (see page 3, 19-20, line 33-38, 302-310 in clean version, and page 3, 19-20, line 89-94, 1270-1344 in the version with tracked changes)

Third, the orientation of this manuscript. Actually, the purpose of this study was to find out whether the placement of the implants affects the surgical outcomes or is it necessary to try to place the implants outside REZ. When we focused only on the difference of the two procedures in the original version, we narrowed the orientation. In the revised version, we reorganized the total manuscript, made detailed descriptions on results and comprehensive assessment on discussions. And the title was revised as: Facial root entry/exit zone contact in microvascular decompression for hemifacial spasm: a historical control study.

Reviewer C

Your research is interesting that 1) MVD was performed successfully without touching REZ by spacer in many patients, and 2) two surgical methods could be compared directly.

However,

1. It is difficult to understand the entire manuscript that acceptance cannot be considered until English editing by experts.

Author response : The entire manuscript has been edited by native English-speaking experts.(see the certificate attached)

2. Do not understand the sentence, "Patients with severe hemifacial spasm may also sustain hearing loss and facial weakness before surgery".

Author response: This sentence and its context were originally intended to express that patients with hearing loss and facial paralysis before surgery were not counted in the postoperative complications. But we did not make it clear. "hearing loss and facial weakness" were not caused by severe hemifacial spasm, they sometimes combined

with severe hemifacial spasm, as patients with severe hemifacial spasm sometimes complain a booming sensation in their ears, and many patients receive botulinum toxin injection and acupuncture before surgery which can lead to facial weakness.

In revised version, this sentence has been removed

3. Fever and vomiting are common immediate postoperative complaints by patients. I disagree with what this is called postoperative complications.

Author response: Thanks for pointing this out. It is inappropriate to define fever and vomiting as the postoperative complications. In the revision, fever and vomiting were defined as postoperative discomforts. (see page 12, line 183-187 in clean version, and page 12, line 789-793 in the version with tracked changes)

4. What is the difference between facial weakness and palsy? If it were same, please use one terminology.

Author response: Strictly, there is no big difference between the two phrases except the severity they represented. In the revision, facial weakness has been replaced by facial palsy.

5. How can you explain that "REZ-undisturbing Decompression" is more surgically difficult than "In-situ Decompression", and it took more surgical time from your data, but the complications were rather less?

Author response: Complications in this study are mainly hearing loss and facial palsy. Analysis on the etiology of these complications has been added in the revised version (see page 16-18, line 244-256, 273-275 in clean version, and page 16-18, line 1121-1133, 1218-1220 in the version with tracked changes). Hearing loss herein was mainly caused by fluid entering the mastoid air cells or direct trauma to the vestibulocochlear nerve, the placement of the implants has little effect on it. While, the "REZ-undisturbing Decompression" certainly has lower incidence of facial palsy, this may be due to the absence of heterogeneous stimulation of implants in facial REZ. And the increasing sophisticated surgical skills may also contribute to it.

6. Delayed facial palsy is known to be more common than immediate facial palsy from previous studies. Why do you think immediate facial palsy is more common in your study?

Author response: Thanks for pointing this out. Many facial palsy in our study was occurred one week after surgery, earlier than the reported. But not all facial palsy was immediate. And the reported onset time of delayed facial paralysis varied in different

studies, ranged from 0-30days (Liu, et al. 2018), 3-16days (Hua, et al. 2016) and 7-23days (Rhee, et al. 2006). Many HFS patients in China receive acupuncture treatment before MVD surgery. Acupuncture would not cause symptoms of palsy, but the muscle weakness and a decreased amplitude of facial compound motor action potential was reported (Zhang, et al. 2019). Thus, the existed facial weakness may be related to the early onset of facial palsy.

Besides, heterogeneous stimulation by implants may also contribute to it.

The related explanation has been added in the revision (see page 17-18, line 257-272 in clean version, and page 17-18, line 1175-1190, 1218-1223 in the version with tracked changes).